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EXAMINER	
DUFFY, BRADLEY	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/826,909	KASIBHATLA ET AL.	
	Examiner	Art Unit	
	Brad Duffy	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-46* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This election/restriction requirement sets forth multiple elections applicable to the Inventions of Groups I-XX (see item nos. 2-9 below).

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I-XXVI. Claims 1, 2, 6-8, 10-13 and 31, drawn to a method of treating, preventing or ameliorating a cancer responsive to induction of the caspase cascade in an animal comprising administering to said animal a xathene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, classified in class 514, subclass 460, for example.

XXVII-LII. Claims 1, 2, 6-8, 10-13 and 31, drawn to a method of treating, preventing or ameliorating a cancer responsive to induction of the caspase cascade in an animal comprising administering to said animal a chromene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, classified in class 514, subclass 453, for example.

LIII-XCIII. Claims 1 and 3, drawn to a method of treating, preventing or ameliorating a disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a compound that binds one Clathrin Heavy Chain Related Apoptosis Inducing Protein from the 41

proteins listed as group C., starting on page 70 of the specification, respectively, classified in class 424, subclass 130.1, for example.

XCIV-CXXII. Claims 1 and 4, drawn to a method of treating, preventing or ameliorating a disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a compound that binds one IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein from the 29 proteins listed as group E., starting on page 73 of the specification, respectively, classified in class 424, subclass 2, for example.

CXXIII-CCXXVIII. Claims 1 and 5, drawn to a method of treating, preventing or ameliorating a disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a compound that binds one Heat Shock Protein Related Apoptosis Inducing Protein from the 106 proteins listed as group G., starting on page 75 of the specification, respectively, classified in class 424, subclass 7, for example.

CCXXIX-CCLIV. Claims 2 and 9, drawn to a method of treating, preventing or ameliorating an inflammatory disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a xathene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, classified in class 514, subclass 183, for example.

CCLV-CCLXXX. Claims 2 and 9, drawn to a method of treating, preventing or ameliorating an inflammatory disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a chromene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, classified in class 514, subclass 449, for example.

CCLXXXI-CCCVI. Claims 14-15 and 19-30, drawn to a method of identifying potentially therapeutic anticancer compounds comprising contacting one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, with test compounds, wherein compounds that bind one Transferrin Receptor Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds, classified in class 435, subclass 7.2, for example.

CCCVII-CCCXLVII. Claims 14 and 16, drawn to a method of identifying potentially therapeutic anticancer compounds comprising contacting one Clathrin Heavy Chain Related Apoptosis Inducing Protein from the 41 proteins listed as group C., starting on page 70 of the specification, respectively, with test compounds, wherein compounds that bind one Clathrin Heavy Chain Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds, classified in class 435, subclass 7.5, for example.

CCCXLVIII-CCCLXXVI. Claims 14 and 17, drawn to a method of identifying potentially therapeutic anticancer compounds comprising contacting one IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein from the 29 proteins listed as group E., starting on page 73 of the specification, respectively, with test compounds, wherein compounds that bind one IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds, classified in class 435, subclass 7.7, for example.

CCCLXXVII-CDLXXXII. Claims 14 and 18, drawn to a method of identifying potentially therapeutic anticancer compounds comprising contacting one Heat Shock Protein Related Apoptosis Inducing Protein from the 106 proteins listed as group G., starting on page 75 of the specification, respectively, with test compounds, wherein compounds that bind one Heat Shock Protein Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds, classified in class 435, subclass 7.8, for example.

CDLXXXIII-DVIII. Claims 32-33, drawn to a method of determining the prognosis efficacy of an anti-cancer Transferrin Receptor Related Apoptosis Inducing Protein binding composition, comprising quantifying the total mRNA of one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, in a cancerous fluid or tissue sample and calculating a ratio comprising the quantity of

said mRNA to the quantity of said mRNA in a normal fluid or tissue, wherein a ratio greater than 1 indicates said binding composition is efficacious, classified in class 436, subclass 94, for example.

DIX-DXXXIV. Claims 34-35, drawn to a method of determining the prognosis efficacy of an anti-cancer Transferrin Receptor Related Apoptosis Inducing Protein binding composition, comprising quantifying the total protein of one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, in a cancerous fluid or tissue sample and calculating a ratio comprising the quantity of said protein to the quantity of said protein in a normal fluid or tissue, wherein a ratio greater than 1 indicates said binding composition is efficacious, classified in class 435, subclass 7.92, for example.

DXXXV-DLX. Claims 36-37, drawn to a complex, comprising one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, and a xanthene Transferrin Receptor Related Apoptosis Inducing Protein binding compound, classified in class 530, subclass 350, for example.

DLXI-DLXXXVI. Claims 36-37, drawn to a complex, comprising one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, and a chromene Transferrin Receptor Related Apoptosis Inducing Protein binding compound, classified in class 530, subclass 352, for example.

DLXXXVII. Claims 38-39, drawn to a xanthene compound, classified in class 549, subclass 200.

DLXXXVIII. Claims 38-39, drawn to a chromene compound, classified in class 532, subclass 1.

DLXXXIX. Claim 40, drawn to a method of identifying potentially therapeutic anticancer compounds comprising, contacting an antibody to gambogic acid or a gamboic acid related compound and determining whether said compound binds said antibody, wherein compounds which bind said antibody are potentially therapeutic anticancer compounds, classified in class 435, subclass 7.1.

DXC. Claim 41-45, drawn to detectably labeled gamboic acid or gambogic acid related compounds, classified in class 532, subclass 16.

DXCI. Claim 46, drawn to a method of bonding *N*-hydroxysuccinimidylgambogate to a solid phase, classified in class 435, subclass 7.72.

3. This application contains claims in Groups I-LII directed to the following patentably distinct species: methods of treating Hodgkin's disease, non-Hodgkin's lymphomas, acute lymphocytic leukemias, chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinomas, ovarian carcinomas, lung carcinomas, Wilms' tumor, cervical carcinomas, testicular carcinomas, soft-tissue sarcomas, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinomas, chronic granulocytic leukemia, primary brain carcinomas, malignant melanoma, small-cell lung carcinomas, stomach carcinomas, colon carcinomas, malignant pancreatic insulinoma,

malignant carcinoid carcinomas, malignant melanomas, choriocarcinomas, mycosis fungoides, head carcinomas, neck carcinomas, osteogenic sarcoma, pancreatic carcinomas, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinomas, thyroid carcinomas, esophageal carcinomas, malignant hypercalcemia, cervical hyperplasia, renal cell carcinomas, endometrial carcinomas, polycythemia vera, essential thrombocytosis, adrenal cortex carcinomas, skin cancer, or prostatic carcinomas.

The species are independent or distinct because they differ in the method objectives. In the instant case, the cancers listed do not have a common origin, a treatment for one would not necessarily work one for the other and the method objectives would be to treat the specific cancer of the patient. Therefore, separate searches would be required to determine patentability for each method of treatment, so restriction as required is proper.

If applicant elects any one of Groups I-LII, applicant is further required under 35 U.S.C. 121 to elect a single cancer that is to be treated from the list above for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 7 is generic for all groups.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consistent with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. If Applicant elects any one of Groups CCXXIX-CCLXXX, Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species given below. Currently, Claim 9 is generic for all groups to the following disclosed patentably distinct species: methods of treating rheumatoid arthritis, multiple sclerosis, insulin-dependent diabetes mellitus, lupus, or muscular dystrophy (see pg. 17 of the specification). The species are independent or distinct because they differ in the method objectives. In the instant case, the inflammatory diseases listed do not have a common origin, a treatment for one would not necessarily work one for the other and the method objectives would be to treat the specific inflammatory disease of the patient. Therefore, separate searches would be required to determine patentability for each method of treatment, so restriction as required is proper. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consistent with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

5. If Applicant elects any one of Groups LIII-CCXXVIII, Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species given below. Currently Claim 3 is generic for Groups LIII-XCIII, Claim 4 is generic for Groups XCIV-CXXII and Claim 5 is generic for Groups CXXIII-CCXXVIII to the following disclosed patentably distinct species: methods of treating Hodgkin's disease, non-Hodgkin's lymphomas, acute lymphocytic leukemias, chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinomas, ovarian carcinomas, lung carcinomas, Wilms' tumor, cervical carcinomas, testicular carcinomas, soft-tissue sarcomas, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinomas, chronic granulocytic leukemia, primary brain carcinomas, malignant melanoma, small-cell lung carcinomas, stomach carcinomas, colon carcinomas, malignant pancreatic insulinoma, malignant carcinoid carcinomas, malignant melanomas, choriocarcinomas, mycosis fungoides, head carcinomas, neck carcinomas, osteogenic sarcoma, pancreatic carcinomas, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinomas, thyroid carcinomas, esophageal carcinomas, malignant hypercalcemia, cervical hyperplasia, renal cell carcinomas, endometrial carcinomas, polycythemia vera, essential thrombocytosis, adrenal cortex

carcinomas, skin cancer, prostatic carcinomas, rheumatoid arthritis, multiple sclerosis, insulin-dependent diabetes mellitus, lupus, or muscular dystrophy (see pg. 17 of the specification). The species are independent or distinct because they differ in the method objectives. In the instant case, the diseases listed do not have a common origin, a treatment for one would not necessarily work one for the other and the method objectives would be to treat the specific disease of the patient. Therefore, separate searches would be required to determine patentability for each method of treatment, so restriction as required is proper. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consistent with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

6. This application contains claims in Groups I-XXVI, Groups CCXXIX-CCLIV, Groups DXXXV-DLX and Group DLXXXVII directed to the following patentably distinct species:

A. 1-allyl-1,3,3a,4,5,12a-hexahydro-7,13-dioxo-1,5-methano-furo[3,4-d]xanthene,

B. 1-allyl-1,3,3 a,4,4a,11a-hexahydro-10,12-dioxo-1,4a-methano-furo[3,4-b]xanthene,

C. 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3 a,4,5,12a-hexahydro-7,13-dioxo-1,5-methano-furo [3,4-d]xanthene, or

D. 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,4a,11a-hexahydro-10, 12-dioxo-1,4a-methano-furo[3,4-b]xanthene,

The species are independent or distinct because they have structural and functional differences. In the instant case, the xanthene compounds listed do not have the same structure, and are disclosed as having functional differences in their ability to induce caspases. Therefore, separate searches would be required to determine patentability for each xanthene compound, so restriction as required is proper.

If applicant elects any one of Groups I-XXVI, Groups CCXXIX-CCLIV, Groups DXXXV-DLX and Group DLXXXVII, applicant is further required under 35 U.S.C. 121 to elect a single disclosed species in the above list from A-D, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 2 is generic for Groups I-XXVI and Groups CCXXIX-CCLIV, Claim 37 is generic for Groups DXXXV-DLX and Claim 38 is generic for Group DLXXXVII.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consistent with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

7. This application contains claims in Groups XXVII-LII, Groups CCLV-CCLXXX, Groups DLXI-DLXXXVI and Group DLXXXVIII directed to the following patentably distinct species:

E. 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a4,510a-hexahydro-7,11-dioxo-9-phenyl-1,5-methano-furo[3,4-i]chromene, or

F. 1-(3-methyl-2-butenyl)-3,3-dimethyl-l,3,3a,4,4a,9a-hexahydro-8,10-dioxo-6-phenyl-1,4a-methano-furo[3,4-g]chromene.

The species are independent or distinct because they have structural and functional differences. In the instant case, the chromene compounds listed do not have the same structure, and are disclosed as having functional differences in their ability to induce caspases. Therefore, separate searches would be required to determine patentability for each chromene compound, so restriction as required is proper.

If applicant elects any one of Groups XXVII-LII, Groups CCLV-CCLXXX, Groups DLXI-DLXXXVI and Group DLXXXVIII, applicant is further required under 35 U.S.C. 121 to elect a single disclosed species in the above list from E-F for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 2 is generic for Groups XXVII-LII and Groups CCLV-

CCLXXX, Claim 37 is generic for Groups DLXI-DLXXXVI and Claim 38 is generic for Group DLXXXVIII.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consistent with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

8. If Applicant elects either Group DLXXXIX or Group DXC, Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species given below. Currently, Claim 40 is generic for Group DLXXXIX and Claim 41 is generic for Group DXC to the following disclosed patentably distinct species: gambogic acid or a gambogic acid related compound (see pg. 21-26 and 28-29 of the specification). Therefore, if Applicant elects either Group DLXXXIX or Group DXC, Applicant must elect either gambogic acid, or one of the gambogic acid related compounds present in the two lists on pages 21-26 and 28-29 of the specification.

The species are independent or distinct because they have structural and functional differences. In the instant case, the compounds listed do not have the same

structure, and are disclosed as having functional differences. Therefore, separate searches would be required to determine patentability for each gambogic acid or gambogic acid related compound, so restriction as required is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consistent with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

9. This application contains claims in Group DXC directed to the following patentably distinct species:

G. N,N-(1,2-aminoethyl)

H. N,N-(2-{2-[2-(2-aminoethoxy)-ethoxy]-ethoxy}-aminoethyl)

I. N,N-(2-[2-(2-aminoethoxy)-ethoxy]-aminoethyl)

J. N,N-[2-(2- {2- [2-(2-aminoethoxy)-ethoxy]-ethylcarbamoyl } -ethyldisulfanyl)-aminoethyl]

K. N,N-(amidoacetamido)

L. N-[(5-{2-[2-(2-aminoethoxy)-ethoxy]-ethylcarbamoyl}-pentyl)-carboxamide]

M. N-({5-[2-(2-aminoethyldisulfanyl)-ethylcarbamoyl]-pentyl})-carboxamide

N. N,N-[(5-aminopentyl)-thioureidyl] or

O. N-({2-[2-(2-aminoethoxy)-ethoxy]-ethyl}-carboxamide).

The species are independent or distinct because they have structural and functional differences. In the instant case, the compounds listed do not have the same structure, and have functional differences in their ability act as linkers. Therefore, separate searches would be required to determine patentability for each linker compound, so restriction as required is proper.

If applicant elects Group DXC, applicant is further required under 35 U.S.C. 121 to elect a single disclosed species in the above list from G-O, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 41 is generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consistent with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after

the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

10. The methods of Inventions of Groups I-XXVI, Groups XXVII-LII, Groups LIII-XCIII, Groups XCIV-CXXII, Groups CXXIII-CCXXVIII, Groups CCXXIX-CCLIV, Groups CCLV-CCLXXX, Groups CCLXXXI-CCCVI, Groups CCCVII-CCCXLVII, Groups CCCXLVIII-CCCLXXVI, Groups CCCLXXVII-CDLXXXII, Groups CDLXXXIII-DVIII, Groups DIX-DXXXIV and Group DLXXXIX differ in the method objectives, method steps, parameters and reagents used. The inventions of Groups I-XXVI recite methods of treating, preventing or ameliorating a cancer responsive to induction of the caspase cascade in an animal comprising administering to said animal a xathene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively. The inventions of Groups XXVII-LII recite methods of treating, preventing or ameliorating a cancer responsive to induction of the caspase cascade in an animal comprising administering to said animal a chromene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively. The inventions of Groups LIII-XCIII recite methods of treating, preventing or ameliorating a disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a compound that binds one Clathrin Heavy Chain Related Apoptosis Inducing Protein from the 41 proteins listed as group C., starting on page 70 of the specification, respectively. The inventions of Groups XCIV-CXXII recite methods of treating, preventing or ameliorating a disease responsive to induction of the caspase cascade in an animal comprising

administering to said animal a compound that binds one IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein from the 29 proteins listed as group E., starting on page 73 of the specification, respectively. The inventions of Groups CXXIII-CCXXVIII recite methods of treating, preventing or ameliorating a disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a compound that binds one Heat Shock Protein Related Apoptosis Inducing Protein from the 106 proteins listed as group G., starting on page 75 of the specification, respectively. The inventions of Groups CCXXIX-CCLIV recite methods of treating, preventing or ameliorating an inflammatory disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a xathene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26. The inventions of Groups CCLV-CCLXXX recite methods of treating, preventing or ameliorating an inflammatory disease responsive to induction of the caspase cascade in an animal comprising administering to said animal a chromene compound that binds one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively. The inventions of Groups CCLXXXI-CCCVI recite methods of identifying potentially therapeutic anticancer compounds comprising contacting one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, with test compounds, wherein compounds that bind one Transferrin Receptor Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds. The inventions of Groups CCCVII-CCCXLVII recite methods of identifying potentially

therapeutic anticancer compounds comprising contacting one Clathrin Heavy Chain Related Apoptosis Inducing Protein from the 41 proteins listed as group C., starting on page 70 of the specification, respectively, with test compounds, wherein compounds that bind one Clathrin Heavy Chain Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds. The inventions of Groups CCCXLVIII-CCCLXXVI recite methods of identifying potentially therapeutic anticancer compounds comprising contacting one IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein from the 29 proteins listed as group E., starting on page 73 of the specification, respectively, with test compounds, wherein compounds that bind one IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds. The inventions of Groups CCCLXXVII-CDLXXXII recite methods of identifying potentially therapeutic anticancer compounds comprising contacting one Heat Shock Protein Related Apoptosis Inducing Protein from the 106 proteins listed as group G., starting on page 75 of the specification, respectively, with test compounds, wherein compounds that bind one Heat Shock Protein Related Apoptosis Inducing Protein are potentially therapeutic anticancer compounds. The inventions of Groups CDLXXXIII-DVIII recite methods of determining the prognosis efficacy of an anti-cancer Transferrin Receptor Related Apoptosis Inducing Protein binding composition, comprising quantifying the total mRNA of one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, in a cancerous fluid or tissue sample and calculating a ratio comprising the quantity of said mRNA to the quantity of said mRNA in a normal fluid or

tissue, wherein a ratio greater than 1 indicates said binding composition is efficacious. The inventions of Groups DIX-DXXXIV recite methods of determining the prognosis efficacy of an anti-cancer Transferrin Receptor Related Apoptosis Inducing Protein binding composition, comprising quantifying the total protein of one Transferrin Receptor Related Apoptosis Inducing Protein from SEQ ID No: 1 to SEQ ID No: 26, respectively, in a cancerous fluid or tissue sample and calculating a ratio comprising the quantity of said protein to the quantity of said protein in a normal fluid or tissue, wherein a ratio greater than 1 indicates said binding composition is efficacious. The invention of Group DLXXXIX recites a method of identifying potentially therapeutic anticancer compounds comprising, contacting an antibody to gambogic acid or a gamboic acid related compound and determining whether said compound binds said antibody, wherein compounds which bind said antibody are potentially therapeutic anticancer compounds. The invention of Group DXCI recites a method of bonding *N*-hydroxysuccinimidylgambogate to a solid phase. Thus, the inventions of Groups I-XXVI, Groups XXVII-LII, Groups LIII-XCIII, Groups XCIV-CXXII, Groups CXXIII-CCXXVIII, Groups CCXXIX-CCLIV, Groups CCLV-CCLXXX, Groups CCLXXXI-CCCVI, Groups CCCVII-CCCXLVII, Groups CCCXLVIII-CCCLXXVI, Groups CCCLXXVII-CDLXXXII, Groups CDLXXXIII-DVIII, Groups DIX-DXXXIV and Group DLXXXIX are separate and distinct in having different method objectives, method steps, parameters and reagents used and different endpoints and are patentably distinct.

The inventions of Groups (I-XXVI), Groups (XXVII-LII), Groups (LIII-XCIII), Groups (XCIV-CXXII), Groups (CXXIII-CCXXVIII), Groups (CCXXIX-CCLIV), Groups

(CCLV-CCLXXX), Groups (CCLXXXI-CCCVI), Groups (CCCVII-CCCXLVII), Groups (CCCXLVIII-CCCLXXVI), Groups (CCCLXXVII-CDLXXXII), Groups (CDLXXXIII-DVIII) and Groups (DIX-DXXXIV) are directed to methods that recite structurally and functionally distinct elements and are not required one for the other. For example, Group I requires SEQ ID NO: 1, Group II requires SEQ ID NO: 2, and so on, which are not required by any of the other groups. Since these proteins are not disclosed as having the same amino acid sequence, a separate search would be required for each sequence. Therefore, since each group requires a structurally and functionally distinct element, Groups (I-XXVI), Groups (XXVII-LII), Groups (LIII-XCIII), Groups (XCIV-CXXII), Groups (CXXIII-CCXXVIII), Groups (CCXXIX-CCLIV), Groups (CCLV-CCLXXX), Groups (CCLXXXI-CCCVI), Groups (CCCVII-CCCXLVII), Groups (CCCXLVIII-CCCLXXVI), Groups (CCCLXXVII-CDLXXXII), Groups (CDLXXXIII-DVIII) and Groups (DIX-DXXXIV) are patentably distinct from each other.

The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, the inventions of Groups I-XXVI, Groups XXVII-LII, Groups LIII-XCIII, Groups XCIV-CXXII, Groups CXXIII-CCXXVIII, Groups CCXXIX-CCLIV, Groups CCLV-CCLXXX, Groups CCLXXXI-CCCVI, Groups CCCVII-CCCXLVII, Groups CCCXLVIII-CCCLXXVI, Groups CCCLXXVII-CDLXXXII, Groups CDLXXXIII-DVIII, Groups DIX-DXXXIV and Group DLXXXIX are patentably distinct.

Inventions of Groups DXXXV-DLX, Groups DLXI-DLXXXVI, Group DLXXXVII, Group DLXXXVIII and Group DXC represent separate and distinct products, which are

made by materially different methods, and are used in materially different methods, which have different modes of operation, different functions and different effects. The xanthene/protein complexes of Groups DXXXV-DLX, chromene/protein complexes of Groups DXXXV-DLX, the xanthene compound of Group DLXXXVII, the chromene compound of Group DLXXXVIII and the gambogic acid or gambogic acid related compound of Group DXC are all structurally and chemically different from each other. A xanthene/protein complex is comprised of a xanthene compound and a protein that binds it, a chromene/protein complex is comprised of a chromene compound and a protein that binds it, a xanthene compound is comprised of a tricyclic ring structure, a chromene is comprised of a bicyclic ring structure and a gambogic acid compound is comprised of a tertracyclic ring structure. While the complexes are all made in binding reactions, the reagents in each reaction are specific for the protein and compound used, so they are all distinct complexes. Additionally, while the compounds are all made by chemical synthesis, they differ in their core structures, so a chemical synthesis reaction that makes one, would not be used to make the others. Furthermore, the complexes could be used in X-ray crystalography methods, the xanthenes could be used to synthesize xanthene related compound, the chromenes could be used to synthesize chromene related compounds and gambogic acid or related compounds could be used to synthesize gambogic acid related compouds. Additionally, complexes of Groups DXXXV-DLX and Groups DLXI-DLXXXVI each contain a different polypeptide corresponding to SEQ ID No: 1 to SEQ ID No: 26, so these groups are distinct from each other and would require separate searches. The examination of all groups would

require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, the inventions of Groups DXXXV-DLX, Groups DLXI-DLXXXVI, Group DLXXXVII, Group DLXXXVIII and Group DXC are patentably distinct.

Inventions of Group DLXXXVII and Groups I-XXVI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the xanthene of Group DLXXXVII could be used in the materially different process of chemically synthesizing related compounds, or the materially different process of treating inflammatory diseases of Groups CCXXIX-CCLIV, both of which differ in the method objective, method steps, parameters and endpoint from the process of treating a cancer and are therefore distinct.

Inventions of Group DLXXXVIII and Groups XXVII-LII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the chromene of Group DLXXXVIII could be used in the materially different process of chemically synthesizing related compounds, or the materially different process of treating inflammatory diseases of Groups CCLV-CCLXX, both of which differ

in the method objective, method steps, parameters and endpoint from the process of treating a cancer and are therefore distinct.

Inventions of Group DLXXXVIII and Groups XXVII-LII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the chromene of Group DLXXXVIII could be used in the materially different process of chemically synthesizing related compounds, or the materially different process of treating inflammatory diseases of Groups CCLV-CCLXX, both of which differ in the method objective, method steps, parameters and endpoint from the process of treating a cancer and are therefore distinct.

11. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter and different searches in the patent literature, restriction for examination purposes as indicated is proper.

12. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise

include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

13. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached at Monday through Friday from 7:00 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Brad Duffy
571-272-9935

David Blanchard
AU 1643